

REMARKS

These remarks are in response to the Office Action mailed November 19, 2002. Claims 171-204 are pending and under examination. Claims 198, 199, 200 and 202 have been cancelled. Claims 171, 178, 181, 188, 195, 203, and 204 have been amended. New claims 205 and 206 have been added. Claims 171-197, 201, and 203-206 are therefore currently pending. Support for new claims 205 and 206 is found in the specification on page 29 at lines 1-4, 8-11, and 21-24.

Claim Rejections under 35 U.S.C. §112, second paragraph

Claim 200 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to recite steps of a “method of harvesting tissue for organ transplantation.” Claim 200 has been cancelled, rendering this rejection moot.

Claim Rejections under 35 U.S.C. §102(e)

Claim 202 was rejected under 35 U.S.C. §102(e) as allegedly anticipated by Falk *et al.* (Pat. No. 5,914,314). Claim 202 has been cancelled, rendering this rejection moot.

Claim Rejections under 35 U.S.C. §103(a)

Claims 171-204 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hamann *et al.* (*J Immunol* (1995) 154(8): 4073-4080, henceforth “Hamann”) in view of Falk *et al.* (Pat. No. 5,827,834, henceforth “Falk”).¹ Applicant respectfully traverses this rejection. Applicant submits that the Examiner has not established a *prima facie* case of obviousness by combining these references and therefore, the rejection under 35 U.S.C. § 103(a) is improper and should be withdrawn.

¹ Hamann is Reference K and Falk is Reference A on PTO Form 892 dated May 8, 2000.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See*, MPEP §§ 2142, 2143. In the present case, none of the criteria for a *prima facie* case of obviousness has been satisfied and therefore, the claim rejection under 35 U.S.C. §103(a) should be withdrawn.

The combination of prior art references do not teach or suggest all the claim limitations

Applicant suggests the requirement that the combination of prior art references must teach or suggest all the claim limitations should be regarded as the threshold criterion for establishing a case of *prima facie* obviousness. If the combination of cited references does not teach the claimed invention, then questions of motivation or suggestion to combine, and reasonable expectation of success, are rendered moot. Therefore, Applicants would like to address this criterion first.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka* 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In the present case, the cited combination of Hamann in view of Falk does not teach all the claim limitations.

Here, the claimed invention teaches a method of releasing cells from bone marrow and other tissue sites, increasing the number of stem cells in the blood, and mobilizing cells, wherein the method comprises administering hyaluronic acid and pharmaceutically acceptable salts thereof. Contrary to the assertion that "Hamann had taught that hyaluronic acid had the activity recited by Applicant" (Office Action, page 5, lines 5-6), Hamman does not disclose releasing cells from bone marrow and other tissue sites, nor increasing the number of stem cells in the blood, nor mobilizing cells. Hamman discloses that HA causes a concentration-related increase in proliferation of CD34⁺ eosinophil progenitor cells. In addition, Applicant is unable to find "the teaching of augmentation of blood cell production taught by Hamann." (OA, page 5, lines

11-12). It is acknowledged that Hamann does not explicitly teach administering hyaluronic acid to a patient. (OA, page 4, lines 14-15). Therefore, Applicant traverses the argument that Hamann "taught that hyaluronic acid had the activity recited by Applicant, and had suggested its therapeutic potential" (OA, page 5, lines 5-7).

Falk allegedly discloses that hyaluronic acid may be administered to patients for various therapeutic purposes, in amounts and molecular weight which encompass those of the claims, and allegedly discloses administration of multiple doses at time intervals. (OA, page 4, lines 16-21). In fact, Falk teaches a method of transporting a non-steroidal anti-inflammatory drug (NSAID) to a site in a patient (Claim 1) and a method of treating side effects expected to arise from administration of NSAID (Claim 2) by topically administering a NSAID and an amount of hyaluronic acid or pharmaceutically acceptable salt thereof in excess of 200 mg (Claim 2). In contrast, the claimed invention does not teach administering a combination of NSAID and hyaluronic acid. Falk teaches and a method of treating anorectal disease by topically administering a combination of a drug useful for treating anorectal disease and hyaluronic acid in a amount that constitutes 2% by weight of the composition (Claim 3). In contrast, the present invention does not teach treating anorectal disease.

In conclusion, the combination of Hamman, in light of Falk, does not teach the claim limitations of the present invention. Because the combination of prior art references does not teach or suggest all the claim limitations, no *prima facie* case of obviousness has been established and the rejection should be withdrawn.

No suggestion or motivation to combine references to make the claimed invention

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q. 2d 1596 (Fed. Cir. 1988); *In re Jones* 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992). See generally, MPEP §2143, especially §2143.01. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's

disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). The argument that a combination is “obvious to try” is not acceptable for establishing obviousness. *In re Tomlinson* 150 U.S.P.Q. 623 (CCPA 1966). Finally, absent a suggestion, teaching, or motivation to combine references, such a combination is unacceptable “hindsight” that does not establish a *prima facie* case of obviousness. *In re Dembiczak* 175 F.3d 994, 50 U.S.P.Q.2d 1614 (Fed. Cir. 1999). In the present case, there is no teaching or suggestion to combine or modify the cited references in such a way as to produce the claimed invention.

Allegedly, an ordinarily skilled worker would have been motivated to administer hyaluronic acid to a patient in order to stimulate production or release of hematopoietic or dendritic cells, including stem cells or red blood cells, “with a reasonable expectation of success because HAMANN had taught that hyaluronic acid had the activity recited by Applicant, and had suggested its therapeutic potential [and] FALK (A) had confirmed that hyaluronic acid could be used therapeutically.” (See, OA, bottom of page 3 to page 5, line 8; quote at page 5, lines 3-8).

As discussed above, Applicant is unable to discern where Hamann taught that hyaluronic acid had the activity recited by Applicant, or where Hamann taught its therapeutic potential. Because Applicant finds no teaching or suggestion in the cited art to combine Hamman and Falk, Applicant finds no motivation to make such a combination. Since the combination of Hamann and Falk do not even teach the claim limitations of the present invention, as discussed above, the Applicant is unable to find motivation to combine Hamann and Falk in the knowledge generally available to one of ordinary skill in the art. Because there is no teaching, suggestion, or motivation to combine the cited references to produce the claimed invention, either in the references themselves or in the knowledge available to one of skill in the art, this criterion for establishing a *prima facie* case of obviousness has not been satisfied, and the rejection should be withdrawn.

No reasonable expectation of success

Prima facie obviousness requires a reasonable expectation of success. In the present case, the cited references provide no reasonable expectation of success. The prior art can be

modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Applicant maintains that the cited references, alone or in combination, do not even teach the claim limitations. Even if, *arguendo*, it were supposed that the cited references taught the claim limitations, the cited references do not provide a reasonable expectation of success because they do not teach or suggest there is any advantage to modifying or combining the steps of these references to produce the claimed invention.

As noted above, Hamann discloses that exposure to HA causes a concentration-related increase in proliferation of CD34⁺ eosinophil progenitor cells *in vitro*, specifically through the CD44 receptor. Applicant is unable to discern where Hamann taught that hyaluronic acid had the activity recited by Applicant, or where Hamann taught its therapeutic potential. Therefore, Applicant finds in Hamann no teaching or suggestion, or reasonable expectation of success, to administer HA as taught in the claimed invention. Falk disclosed topical administration of a combination of NSAID or a drug useful for treating anorectal disease, and HA or a pharmaceutically acceptable salt thereof. Applicant finds in Falk no teaching or suggestion, or reasonable expectation of success, to administer HA as taught in the claimed invention. Because there is no reasonable expectation of success from combining the cited references to produce the invention of Claims 171-204, this criterion for establishing a *prima facie* case of obviousness has not been satisfied, and the rejection should be withdrawn.

Regarding the Mehl/Biophile citation

In the Office Action mailed November 19, 2002, *Mehl/Biophile International Corp. v. Milgram* (52 U.S.P.Q.2d 1303 (Fed. Cir. 1999), henceforth *Mehl/Biophile*) is cited to support the position that Applicant's earlier argument that neither Hamann nor Falk teaches release or mobilization of cells is allegedly "not relevant to the inquiry at hand that HAMANN and FALK

may not have recognized this particular benefit of administration of hyaluronic acid, because HAMANN suggests and FALK teaches in vivo administration.” (OA, page 5, lines 8-12).

Applicants point out that *Mehl/Biophile* was concerned with interpretation of 35 U.S.C. §102, with respect to questions of anticipation, identity of elements, and inherency in the prior art. In contrast, Applicant’s earlier argument that neither Hamann nor Falk teaches release or mobilization of cells was made as part of a nonobviousness argument in the Response to Office Action filed March 13, 2003. However, the question of whether the holding in *Mehl/Biophile* regarding inherency under 35 U.S.C. §102 can be applied to a nonobviousness argument is moot, since neither Hamann nor Falk, alone or in combination, teach the claim limitations of the present invention.

Summary regarding obviousness

In sum, no *prima facie* case of obviousness has been established. The cited references fail to teach or suggest all the claim limitations of Claims 171-204. In addition, the cited references fail to teach or suggest combining or modifying the references to produce the claimed invention, or provide guidance as to how to combine or modify references to produce the claimed invention. Finally, the cited references fail to provide reasonable expectation of success from combining or modifying the methods in the cited references. Thus, it cannot objectively be stated that the skilled artisan could combine or modify the references in such a way as to produce the claimed methods, let alone that the skilled artisan would be motivated to combine these references or that there would be a reasonable expectation of success. Because none of the criteria for establishing a *prima facie* case of obviousness has been satisfied, the rejection under 35 U.S.C. §103(a) is improper and must be withdrawn.

CONCLUSION

Claims 171-204 are pending. Claims 171-204 were rejected in the Office Action mailed November 19, 2002. Claims 198, 199, 200 and 202 have been cancelled. Claims 171, 178, 181, 188, 195, 203, and 204 have been amended. Claims 205 and 206 have been added. Claims 171-197, 201, and 203-206 are therefore currently pending. Applicant requests entry of claim

amendments and new claims. Applicant requests that claim rejections be reconsidered and withdrawn in light of the foregoing remarks, and that pending claims be found in condition for allowance.

If the Examiner believes that a telephone interview would expedite prosecution of this application, she is encouraged to telephone the undersigned Applicant's attorney.

If the fee authorized is incorrect or if any other fees are due in connection with this submission, please charge any such fee or credit any overpayment to Deposit Account No. 03-3975.

Respectfully submitted,

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